

Using Circadian Heart Rate to assess the Impact of Chronic Stress and Mental Health

March 2016

medibio[∞]
INNOVATION IN MIND

We believe individuals, families and carers
affected by mental health can live full,
happy & healthy lives.

Redefining mental health by making the intangible, tangible.

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Company Summary

- Medibio's digital mental health platform will transform the assessment and management of mental health
- Defensible IP/technology based on 20 years of research into the relationship between the autonomic nervous system and mental health
- Support of notable research partners- Johns Hopkins University, Mayo Clinic, Emory University, Ottawa University, BMRI
- FDA submission this year and existing reimbursement codes to pave the way for clinical and corporate acceptance
- Multiple commercialisation routes – Clinical, Pharma, B2B and B2C represent multi-billion dollar market opportunities
- B2B product on market now and in use with key strategic partners

“It is critical to realise that we cannot succeed if we use DSM categories as the gold standard. We need a quantitative method for diagnosing depression.”

(U.S. National Institute of Mental Health - 2013)

“The Single Greatest Illness that Affects Mankind” *

- Neuropsychiatric disorders are the leading cause of disability in the U.S.

- WHO estimates the global cost of mental illness as \$2.5T in 2010 (est. \$6T in 2030)

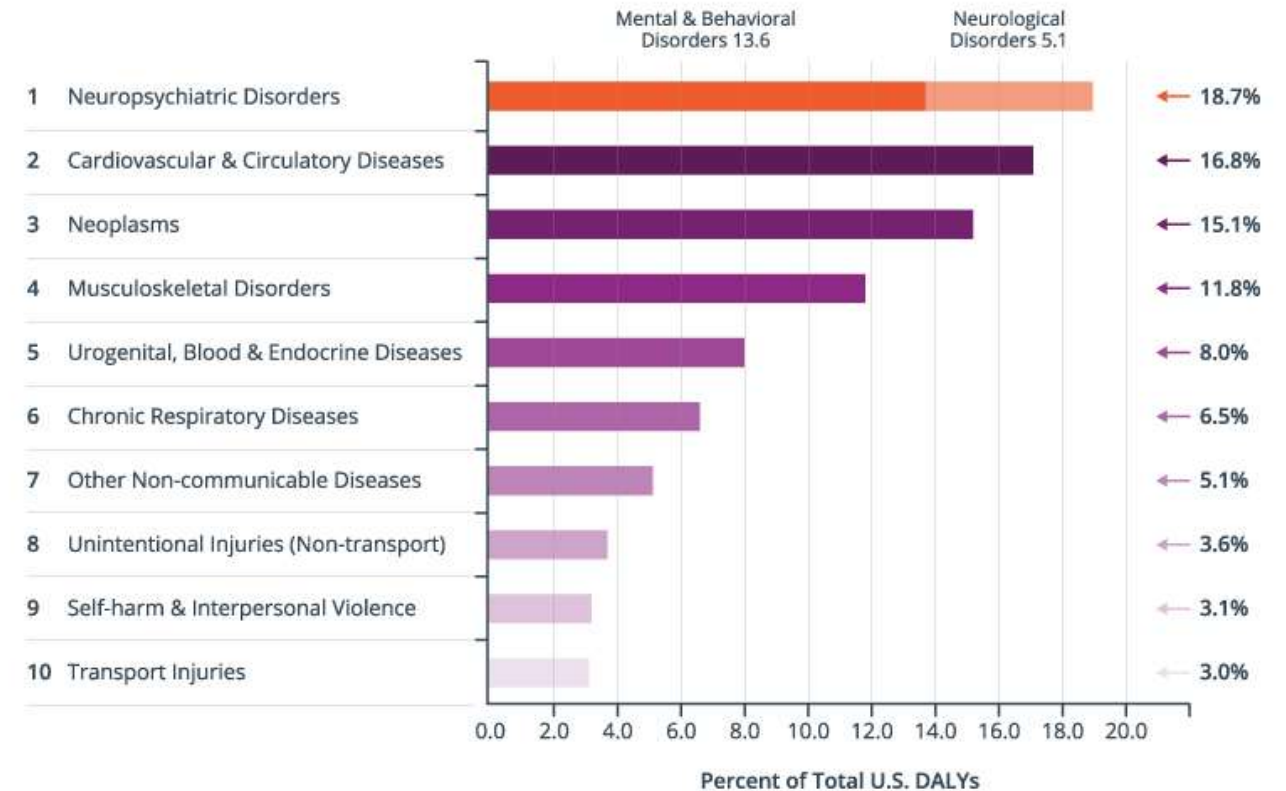
References

- NIMH [article](#)
- World Health Organization. (WHO 2011a). *Global status report on non-communicable diseases 2010*. Geneva: WHO

- * World Mental Health Day 2015
Professor [Stephen Lawrie, Head of Psychiatry at Edinburgh](#)

Data courtesy of WHO

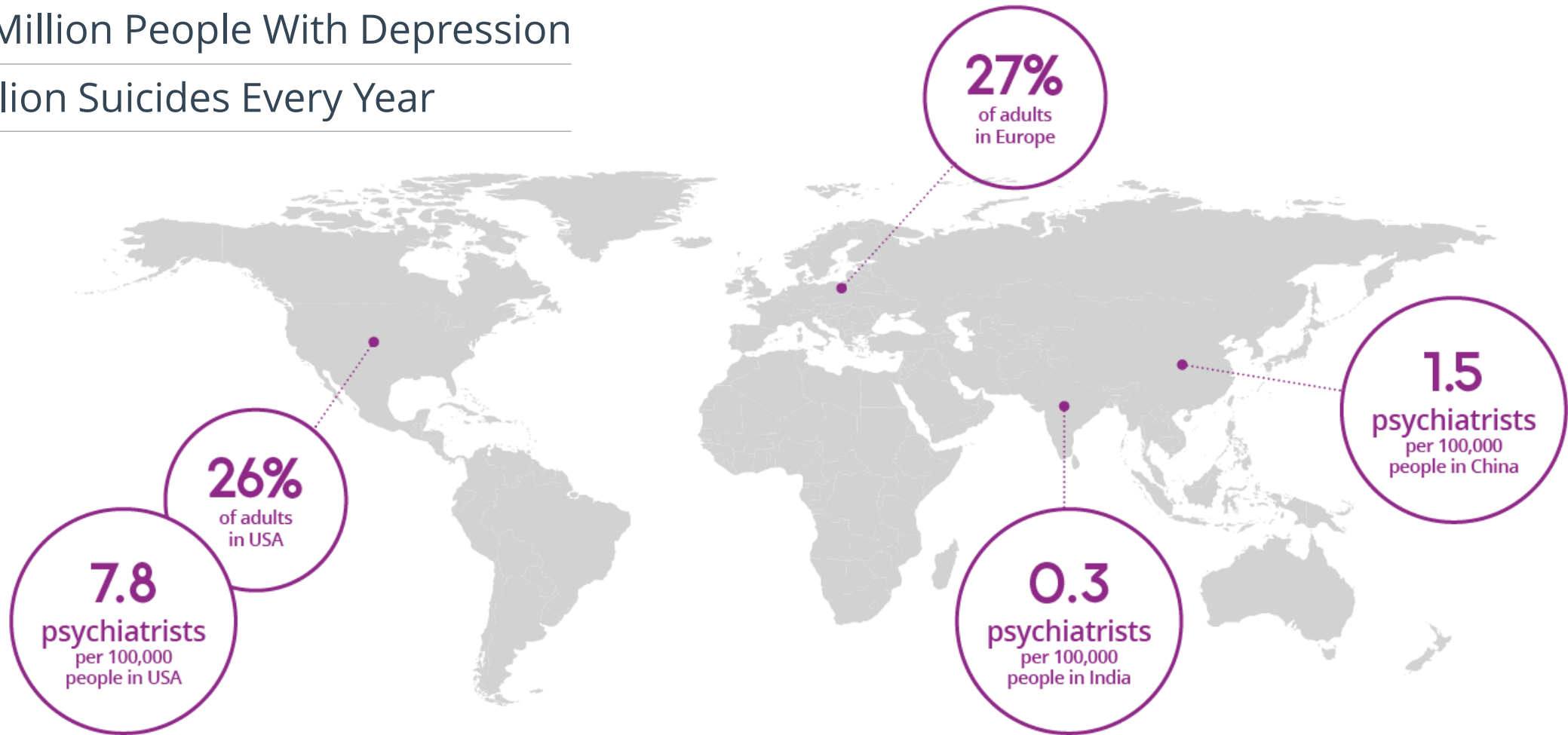
Top 10 Leading Disease/Disorder Categories Contributing to U.S. DALYs (2010)



A Global Crisis of Access & Management

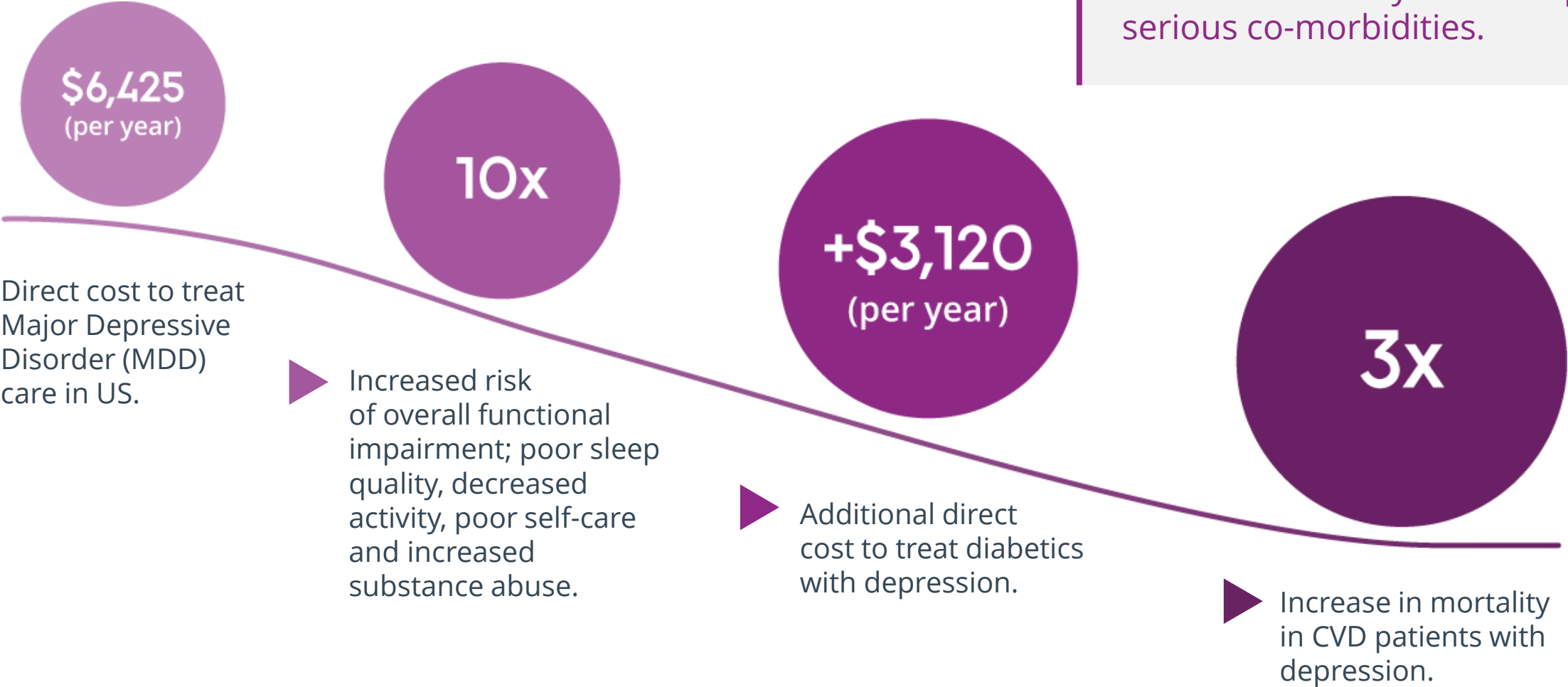
350 Million People With Depression

1 Million Suicides Every Year



Snowball Effect of Depression

Patients diagnosed with MDD are far more likely to develop serious co-morbidities.



The Need for Objectivity

“The economic costs of mental illness will be more than cancer, diabetes & respiratory ailments put together.”

Thomas Insel, MD – Former Director National Institute of Mental Health

Current Pain Points

- No objective test for mental illness.
- The diagnostic “gold standard” is a clinical/expert opinion.
- Diagnostic agreement between clinicians can vary considerably – concordance rates near 70%.
- Current assessments are subjective which can lead to inadequate or incorrect diagnosis.
- Misdiagnosis of depression (and other mental illness) places a huge cost burden on the healthcare system and the workplace.

Medibio’s Solution

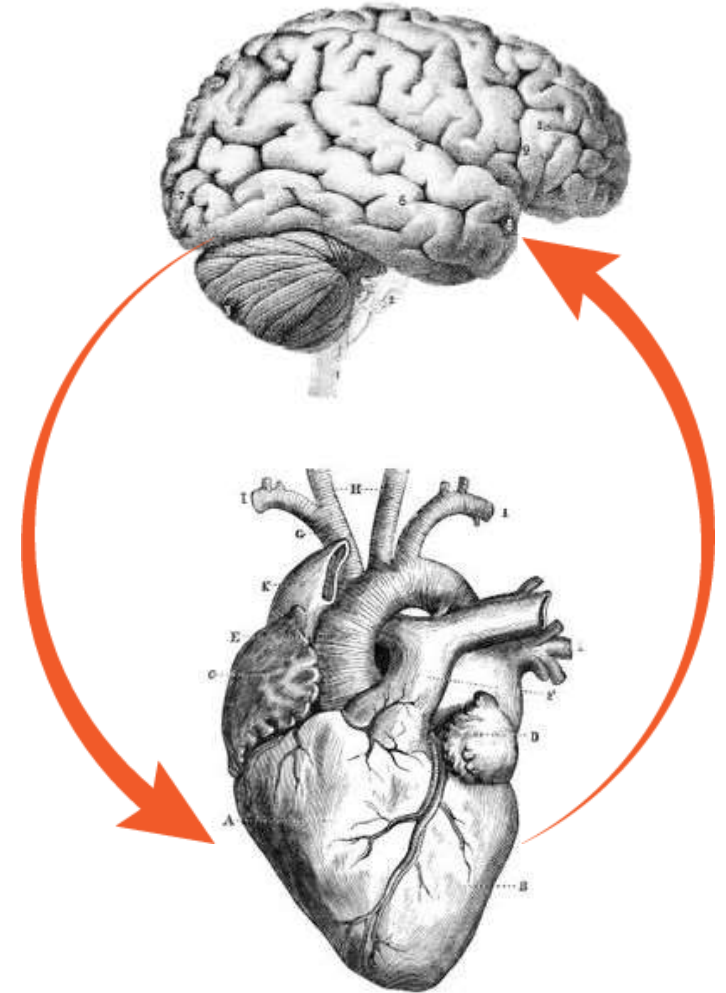
- Quantitative, objective test.
- Diagnosis based on patient’s biometric data (circadian heart rate waveform).
- Repeatable, reliable test with classification accuracy of >80%.
- Provides objective indication of treatment efficacy along with medication compliance and adherence.
- Savings to the health system and better patient outcomes.

Medibio's
Digital Mental Health Platform
will transform the assessment
and management of mental
health by:

- Enabling access to care
- Providing objective, quantifiable diagnosis
- Confirming the effectiveness of therapies
- Driving optimal disease management

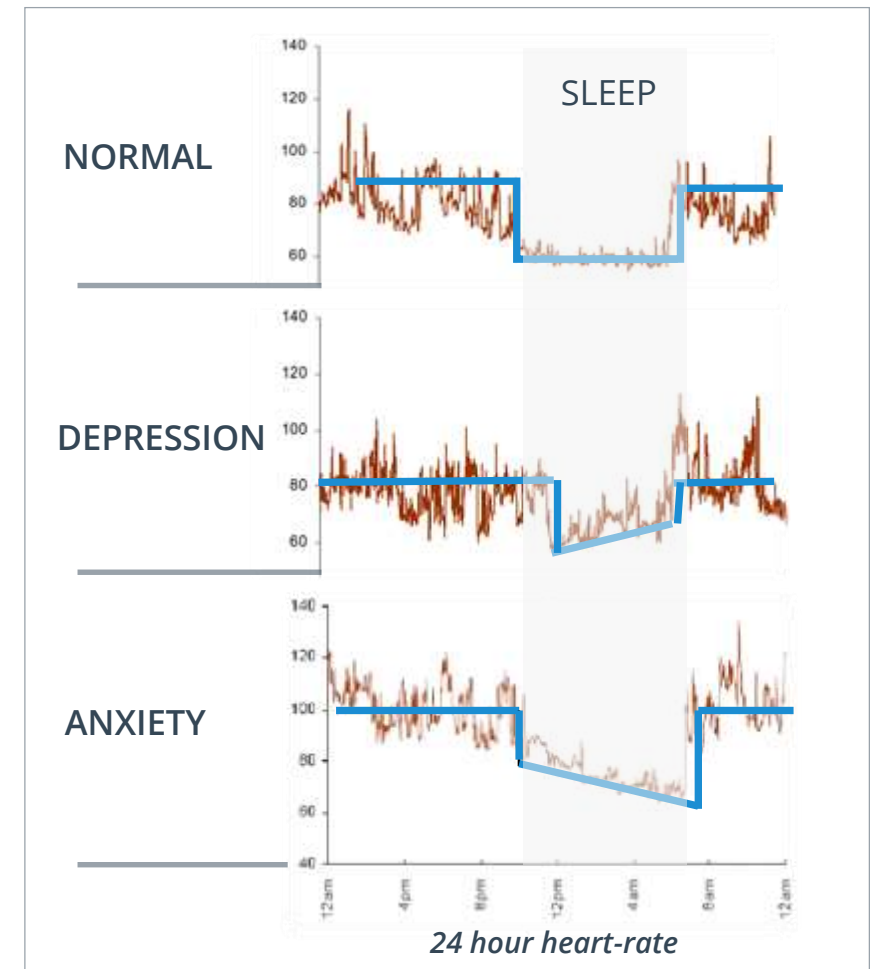
The Mind-Heart Link

- The psychosomatic link between the heart and emotion has been recognized since antiquity and is embedded in language ('made my heart skip a beat... heart broken... cold hearted')
- 5000 years ago, Ayurvedic physicians diagnosed mental illness by feeling a person's pulse!
- The heart is not merely a pump. It has a neuronal circuitry of around 40000 neurones, secretes hormones [A&B natriuretic, norepinephrine & dopamine (ICA cells), oxytocin], has endocrine receptors and has dense interconnections with different parts of the brain.
- The autonomic nervous system (ANS) plays a key role in circadian sleep-wake regulation which includes heart rate.
- All serious mental illness (SMI) are associated with ANS and wider neuroendocrine dysregulation (especially affective disorders) and abnormalities in circadian regulation.



Insights Based on 20 years of Clinical Experience

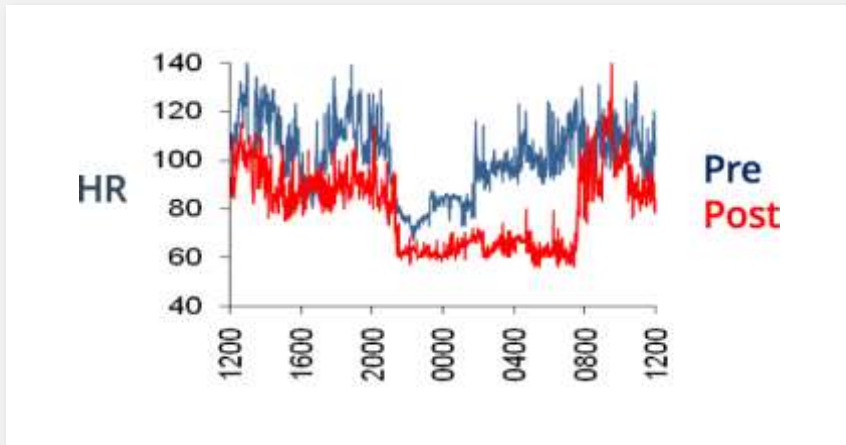
- Research initiated 20 years ago at University of Western Australia to test the theory that mental state linked ANS disturbance could be observed via the cardiovascular system.
- Mental state-linked ANS disturbance is observed via the cardiovascular system during sleep when external influences are absent.
- Morphologic analysis of circadian heart rate waveforms (CHR) gives objective indications of 'core' physiological differences between different forms of mental illness such as anxiety, depression, and stress.
- Serial monitoring of patients under psychiatric treatment showed that effective intervention is associated with normalisation of CHR, providing a tool for determining treatment effectiveness.



Objective Assessment of Therapy Effectiveness

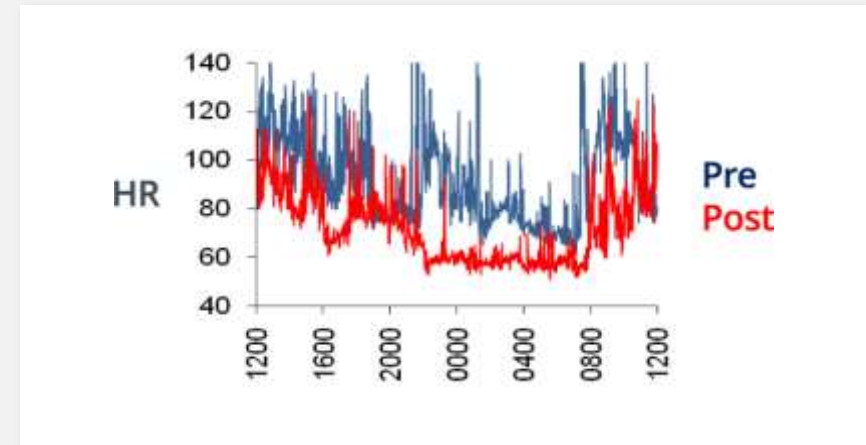
Case Study 1

- Depressed individual upon initial diagnosis
- Treated for 18 days with:
 - Olanzapine – 10mg (night)
 - Mirtazapine – 60mg (night)



Case Study 2

- Individual diagnosed with Generalized Anxiety Disorder (GAD)
- Re-evaluated 10 days following effective treatment



Significant Validation Supporting Technology

CLASSIFICATION ACCURACY	STUDY OUTLINE	REFERENCE
98%	32 controls (normals) and 28 with either an affective disorder or a psychotic disorder	International Congress on Schizophrenia - 2003
78%	50 across the mental health continuum	Psychiatric Quarterly, Vol. 73, No. 3, Fall 2002 (2002)
80%	98 patients, mixed psychopathology and normals	Diligence by UNSW and Newcastle University independent researchers
82%	200 patients, 30 normals, 30 depression, 30 GAD, 110 other mixed psychopathologies	Australian & New Zealand Journal of Psychiatry 1998; 32; 187-198

Defensible Position Based on Decades of Research



Comprehensive suite of patents around CHR & technology:

- Medical diagnostics including assessment of treatment efficacy
- Stress assessment



Patent suite for medical diagnostics includes:

- Method for Diagnosing Psychiatric Disorders
- Method and System for Monitoring Stress Conditions covering the use of CHR for stress assessment
- Method and System for using CHR to Diagnose Psychiatric Disorders



Proprietary data set required is the natural protection:

- 10,000+ 12 hour ECG files with a corresponding psychiatric diagnosis
- This data set would take 5 years and cost \$20 million to replicate

Opportunities in Multiple Broad Markets

REGULATED

UNREGULATED

MEDICAL

US \$30Bn Industry



- Primary Care Physicians
- Psychiatrists
- Psychologists
- Therapists
- Counsellors
- Cardiologists

PHARMA

US \$76Bn Industry



- Global Pharma companies
- Clinical trial organizations
- Companion diagnostics

B2B

US \$19Bn Industry



- High Risk Occupations
 - Defence
 - Police/Fire/Emergency
- Govt / Corporate Wellness
- SME Health and Wellbeing
- Elite Sports

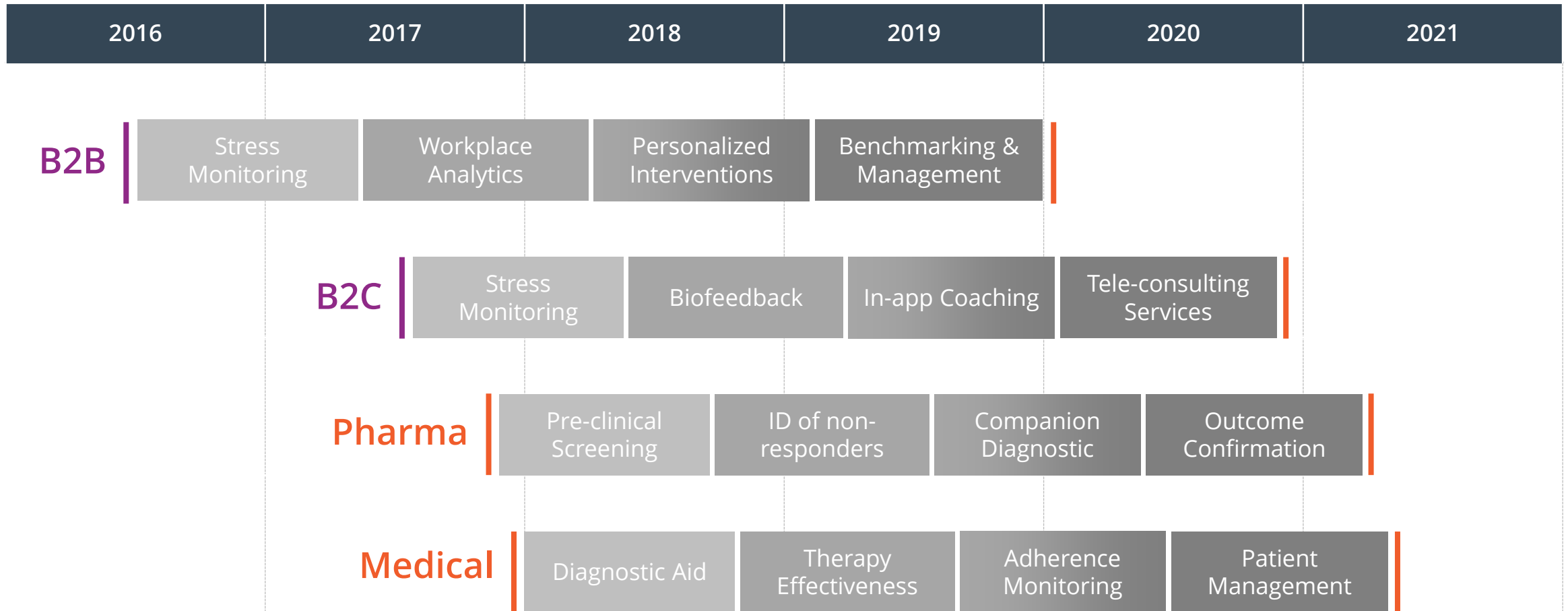
B2C

US \$26Bn Industry



- Direct to Consumer
- Insurance Companies
- Wellness Providers
- Digital Health Companies

Robust Roadmap into Multi-billion \$ Verticals



Significantly Improving the Patient Journey

Typical MDD Patient Journey \longrightarrow Years to Proper Treatment

Developing Condition	Undiagnosed Condition	Diagnosis	Treatment Titration	Management
Variable	3-6 months	3-6 months over multiple doctor visits	3-6 months over multiple doctor visits	Episodic doctor visit every 3-6 months



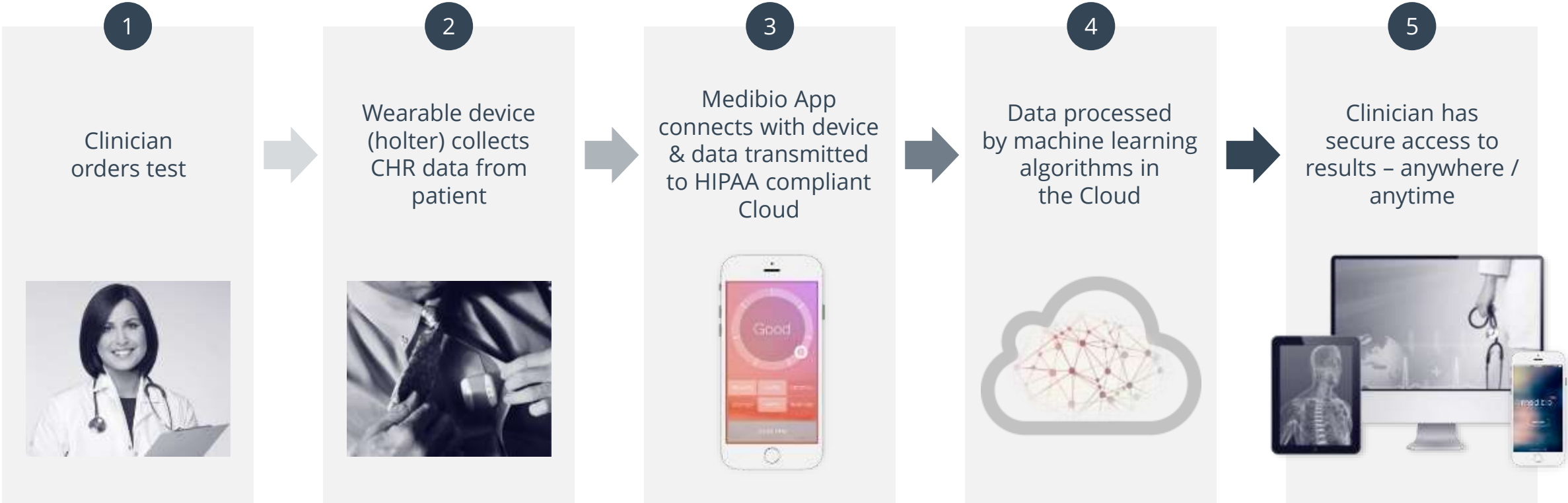
Digital Mental Health \longrightarrow Continuous & Real-time

Monitoring & Diagnosis	Treatment Titration	Management
Continuous feedback & diagnosis	Remote, daily feedback on drug effectiveness	Continuous feedback & management / data-based doctor visits

\$3,000/yr

Difference in annual direct costs between managed and unmanaged depression.

Clinical Work Flow



Clinical Market Opportunity

- PCP's in the US are becoming the primary psychiatric care provider with in excess of **50% of all psychiatric diagnosis**
- Of the **21 million annual** PCP visits in the US which are mental health related:
 - **40%** receive only psychiatric medication
 - **30%** receive medication and are given some therapy
 - **30%** are referred to a psychiatrist/psychologist
- Will be marketed as a **diagnostic aid with the early adopter** PCPs
- Model based on the current structure for ambulatory ECG monitoring

CPT CODE	MEDICARE	PRIVATE	INSURANCE
93225	Recording (Provider)	\$26.87	\$40
93226	Analysis with Report (Medibio)	\$37.91	\$57
93227	Physician review and Interpretation (Provider)	\$26.87	\$40

- PCP Initial diagnostic market – 21 million annual PCP visits @ \$45 **\$1 billion annually (TAM)**
- Ongoing monitoring – 16 million with depression in US quarterly @ \$22.50 **\$1.6 billion annually (TAM)**
- **5% penetration of the US market** for depression diagnosis would generate revenue **of \$175 million annually**
- Cloud based analysis and reporting = minimal costs per report = **very high margins**

Corporate Wellness is a Large & Growing Market

Value Proposition

- **43%** of the adults in the US suffer adverse health effects from stress
- Stress is estimated to cost US employees **\$300 billion** annually
- Over half of the **550 million** working days lost annually in the U.S.
- Stress is estimated to cause 30% of employee turnover

US Market Size

- **54 million** employees in the US (+1,000 staff firms³)
- **90%** of corporates have an existing wellness program
- Annual wellness spend **\$100-\$500** per employee, **US\$4BN** revenue potential

Go to market strategy

- Partner with existing participants in the Corporate Wellness market
- Medibio will provide data analytics and reporting – our core competency

1. www.stress.org/workplace-stress
2. www.evancarmichael.com/Work-Life/1877/Less-Stress-More-Profit--the-Value-of-Corporate-Stress-Management-Training.html
3. US Census



Starbucks spends more on employee benefits than on coffee.



Of chief financial officers cited healthcare costs as their main financial concern.



SOLUTION
\$1 spent on health promotion & disease prevention =
\$5 decrease
in overall medical costs.

Aggressive Revenue Growth Potential

- Service delivery model through Wellness Channel partners
- Medibio as a catalyst for changing business models (e.g. Digital)
 - Enable innovation
 - Increased use of Services (Existing/New)
 - Broader coverage of Services (Existing/New)
- Subscription pricing model
 - Stress Monitoring
 - User Analytics
 - Client Analytics
 - Provider Analytics
- **5% penetration of the US market would generate \$247 million annual revenue**



B2C Market Opportunity

All Apps related to stress/mental health are:

- based on reducing tension via breathing, yoga, and relaxing sounds
- mental health Apps are based on a digitised version of the DSM
- **none offer objective stress assessment based on extended research**

Medibio's App

- An health sector endorsed, objective stress assessment application and management tool
- Integration testing with popular wearable devices underway as a precursor to commercial launch decision

Business Model

- Initial download cost gives you a month of complete usage including the stress management interventions
- Subscription based model for a 12 month
- Nearest competitor is "Stress Doctor" which has generated 60+ million iOS downloads
 - Current Price US\$7.99



Key Company Milestones

TIMING	MILESTONE	STATUS
Q1 2016	Commence commercial stress pilots (2 separate customers)	✓
	FDA Feedback on Pre-submission package	
Q2 2016	Completion of wearable testing program with NTICA	
	Announcement of Foundation Partner for Australian Corporate Stress Rollout	
	Start Independent Validation Study Corporate Stress product	
	Completion of commercial stress pilots (2 separate pilots)	
Q3 2016	Binding Commercial Agreement with Medtronic	
	Decision on launch of Consumer Stress App	
	Announcement of second Regional Foundation Partner	
Q4 2016	Completion of John Hopkins University Validation Study	
	Lodgement of FDA Application (Depression Diagnostic)	
	Results from University of Ottawa Study	



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